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## **ELECTRONIC SUPPLEMENTARY INFORMATION**

### **Highly Enantioselective Cu-catalysed Allylic Substitutions with Grignard Reagents**

Fernando López, Anthoni W. van Zijl, Adriaan J. Minnaard, Ben L. Feringa\*

*Department of Organic Chemistry and Molecular Inorganic Chemistry, Stratingh Institute,  
University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands*

**General Procedures:**  $^1\text{H}$  NMR spectra were recorded at 300 or 400 MHz with  $\text{CDCl}_3$  as solvent.  $^{13}\text{C}$  NMR spectra were obtained at 75.4 or 100.59 MHz in  $\text{CDCl}_3$ , (Varian VXR300 or AMX400 spectrometers). Carbon types were determined from APT  $^{13}\text{C}$  NMR experiments. Chemical shifts were determined relative to the residual solvent peaks ( $\text{CHCl}_3$ ,  $\delta = 7.26$  ppm for hydrogen atoms,  $\delta = 77.0$  for carbon atoms). The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Progress and conversion of the reaction was determined by GC-MS (GC, HP6890; MS HP5973) with an HP1 or HP5 columns (Agilent Technologies, Palo Alto, CA). Enantio- and regioselectivities were determined by capillary GC analysis (HP 6890, ChiralDEX G-TA column (30 m x 0.25 mm), CP-Chiralsil-Dex-CB (25 m x 0.25 mm)) using flame ionization detector (in comparison with racemic products). Optical rotations were measured in  $\text{CHCl}_3$  on a *Schmidt + Haensdch* polarimeter (Polartronic MH8) with a 10 cm cell (*c* given in g/100 mL). Absolute configuration of the products was determined by comparison with compounds previously published. Thin-layer chromatography (TLC) was performed on commercial Kieselgel 60F<sub>254</sub> silica gel plates, and components were visualized with  $\text{KMnO}_4$  reagent. Flash chromatography was performed on silica gel. Drying of solutions was performed with  $\text{Na}_2\text{SO}_4$ . Concentrations were conducted with a rotary evaporator.

Ligands **1a-1b** were generously donated by Solvias.<sup>1</sup> Ligand Taniaphos (**2**) was prepared according to literature procedures.<sup>2</sup>  $\text{CuCl}$ ,  $\text{CuI}$ , and  $\text{CuBr SMe}_2$  were purchased from Aldrich or Acros, and used without further purification. CuTC refers to copper thiophene-2-carboxylate.<sup>3</sup> Hoveyda-Grubbs 2<sup>nd</sup> generation catalyst,<sup>4</sup> (*E*)-cinnamyl bromide (**3a**) and (*E*)-cinnamyl chloride (**3b**) were purchased from Aldrich. The substrates **3b**,<sup>5</sup> **3d-3f**,<sup>6</sup> **3g**,<sup>7</sup> and **3h**<sup>8</sup> were prepared according to literature procedures. Grignard reagents were purchased from Aldrich ( $\text{EtMgBr}$ ,  $\text{MeMgBr}$ ) or prepared from the corresponding alkyl bromides and magnesium turnings in  $\text{Et}_2\text{O}$  following standard procedures. Grignard reagents were titrated using  $^t\text{BuOH}$  and catalytic amounts of 1,10-phenanthroline.  $^t\text{BuOMe}$  was purchased as anhydrous grade, stored over 4 Å MS and used without further purification.  $\text{Et}_2\text{O}$  was distilled from Na/benzophenone.  $\text{CH}_2\text{Cl}_2$  was distilled from  $\text{CaH}_2$ . All reactions were conducted under argon atmosphere using standard Schlenk techniques.

Racemic products **4** and regioisomers **5** were obtained by reaction of the bromides **3** with the corresponding Grignard reagent (5.0 equiv) at  $-25^\circ\text{C}$  in  $\text{CH}_2\text{Cl}_2$  in the presence of CuCN (100 mol %). In some cases, the racemic products were also obtained by using *racemic-2* ligand, following the general procedure described in the next page.

Spectroscopic and analytical data of products **4b**, **4e-h** were obtained from their mixtures with **5**. The products **4a-4l**, and **6** have been previously described (see appropriate references in the following pages).

<sup>1</sup> A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, *J. Am. Chem. Soc.*, 1994, **116**, 4062.

<sup>2</sup> T. Ireland, G. Grossheimann, C. Wieser-Jeunesse, P. Knochel, *Angew. Chem. Int. Ed.*, 1999, **38**, 3212.

<sup>3</sup> G. D. Allred, L. S. Liebeskind, *J. Am. Chem. Soc.*, 1996, **118**, 2748.

<sup>4</sup> S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.*, 2000, **122**, 8168.

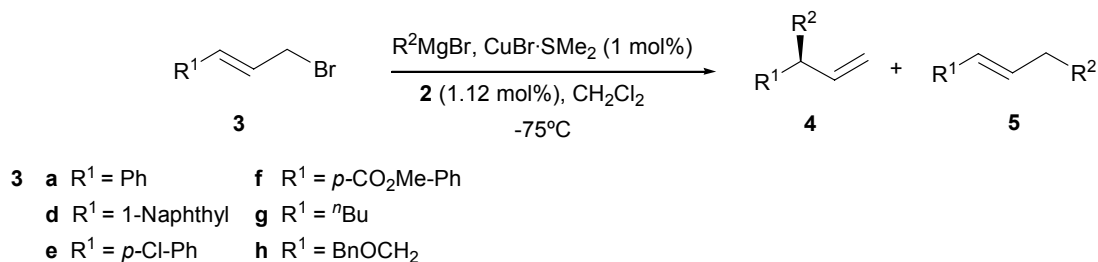
<sup>5</sup> C. A. Luchaco-Cullis, H. Muzitani, K. E. Murphy, A. H. Hoveyda, *Angew. Chem. Int. Ed.* 2001, **40**, 1456.

<sup>6</sup> A. W. van Zijl, L. A. Arnold, A. J. Minnaard, B. L. Feringa, *Adv. Synth. Catal.*, 2004, **346**, 413 and references therein.

<sup>7</sup> M. R. Binns, R. K. Haynes, D. E. Lambert, P. A. Schober, S. G. Turner, *Aust. J. Chem.*, 1987, **40**, 281.

<sup>8</sup> G. Kottirsch, G. Koch, R. Feifel, U. Neumann *J. Med. Chem.*, 2002, **45**, 2289.

## General Procedure for the Enantioselective Cu-catalysed Allylic Alkylation with Grignard Reagents



In a Schlenk tube equipped with septum and stirring bar, CuBr SMe<sub>2</sub> (15.0 μmol, 3.08 mg) and ligand **2** (18 μmol, 12.4 mg) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (3.0 mL) and stirred under argon at room temperature for 10 min. The mixture was cooled to – 75 °C and the corresponding Grignard reagent (solution in Et<sub>2</sub>O, 1.73 mmol) was added dropwise. Allylic bromide **3** (1.50 mmol) was then added dropwise as a solution in CH<sub>2</sub>Cl<sub>2</sub> at that temperature over 15 min *via* a syringe pump. Once the addition was complete the resulting mixture was further stirred at – 75 °C for 4-12h. The reaction was quenched by addition of MeOH (0.5 mL) and the mixture was allowed to reach rt. Then, aqueous NH<sub>4</sub>Cl solution (1M, 2 mL) was added to the mixture. The organic phase was separated, and the resulting aqueous layer is extracted with Et<sub>2</sub>O (0.5 mL, 3x). The combined organic phases were dried and concentrated to a yellow oil which was flash chromatographed (2 : 98 Et<sub>2</sub>O/pentane) to yield the corresponding allylic substrates as a mixture of S<sub>N</sub>2' (**4**) and S<sub>N</sub>2 (**5**) regioisomers.

**Note:** GC analysis was carried out on a sample obtained after aqueous extraction with Et<sub>2</sub>O, which has been passed through a short plug of silica gel to remove transition metal residues.

**(+)-1-((S)-but-3-en-2-yl)benzene (4a):**<sup>9</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 97 : 3 mixture of **4a** and **5a** as a colorless oil. [91% yield, **4a**: 98% ee, [α]<sub>D</sub> = +5.4 (*c* 1.2, CHCl<sub>3</sub>), lit.<sup>9a</sup> (81% ee) [α]<sub>D</sub> = + 4.8 (neat), lit.<sup>9b</sup> for (**R**)-**4a** (60% ee) [α]<sub>D</sub> = –2.2 (*c* 0.7, CHCl<sub>3</sub>)]. **4a**: <sup>1</sup>H-NMR δ 7.28-7.14 (m, 5H), 6.02-5.93 (m, 1H), 5.04-4.98 (m, 2H), 3.47-3.40 (m, 1H), 1.33 (d, *J* = 7.0 Hz, 3H); <sup>13</sup>C-NMR δ 145.5 (C), 143.2 (CH), 128.3 (CH), 127.2 (CH), 126.0 (CH), 113.0 (CH<sub>2</sub>), 43.1 (CH), 20.7 (CH<sub>3</sub>). Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 75 °C, retention times (min): 15.6 (minor) and 15.8 (major); Retention time **5a**: 23.7 min.

**(+)-1-((S)-pent-1-en-3-yl)benzene (4b):**<sup>10</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 81 : 19 mixture of **4b** and **5b** as a colorless oil.

<sup>9</sup> (a) T. Hayashi, M. Konishi, M. Fukushima, K. Kanehira, T. Hioki, M. Kumada, *J. Org. Chem.*, 1983, **48**, 2195. (b) M. Kawatsura, Y. Uozumi, M. Ogasawara, T. Hayashi, *Tetrahedron*, 2000, **56**, 2247.

<sup>10</sup> (a) A. W. van Zijl, L. A. Arnold, A. J. Minnaard, B. L. Feringa, *Adv. Synth. Catal.*, 2004, **346**, 413. (b) K. Tissot-Croset, D. Polet, A. Alexakis, *Angew. Chem., Int. Ed.*, 2004, **43**, 2426. (c) A. Alexakis, K. Tissot-Croset, *Org. Lett.*, 2002, **4**, 4147. (d) M. A. Kacprzyński, A. H. Hoveyda, *J. Am. Chem. Soc.*, 2004, **126**, 10676.

[92% yield, **4b**: 95% ee,  $[\alpha]_D = +47$  ( $c$  1.0,  $\text{CHCl}_3$ ), lit.<sup>10b</sup> (96% ee)  $[\alpha]_D = +55$  ( $c$  1.1,  $\text{CHCl}_3$ ); lit.<sup>10d</sup> for (**R**)-**4b** (95% ee)  $[\alpha]_D = -51$  ( $c$  0.5,  $\text{CHCl}_3$ )]. **4b**:  $^1\text{H-NMR}$   $\delta$  7.32-7.12 (m, 5H), 5.91 (m, 1H), 5.01-4.97 (m, 2H), 3.11 (q,  $J = 7.4$  Hz, 1H), 1.74-1.64 (m, 2H), 0.83 (t,  $J = 7.31$  Hz, 3H);  $^{13}\text{C-NMR}$   $\delta$  144.4, 142.2, 128.4, 127.6, 126.1, 114.0, 51.7, 28.3, 12.1.. LRMS (EI)  $m/z$  146 ( $\text{M}^+$ , 32), 128 (10), 117 (100), 91 (62). Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 75 °C for 30 min, then 5 °C/min to 100 °C (final temp), retention times (min): 26.0 (minor) and 26.2 (major); Retention time **5b**: 38.0 min.

**(R)-3-methylhept-1-ene (4c)**:<sup>11</sup> Reaction carried out using 5.0 mol%  $\text{CuBr}\cdot\text{SMe}_2$  and 6.0 mol% **2**. Reaction time: 12 h. Purification by column chromatography (2 : 98  $\text{Et}_2\text{O}$ /pentane) afforded a 100 : 0 mixture of **4c** and **5c** as a colorless oil. [99% conversion,<sup>12</sup> 92% ee].<sup>13</sup> **4c**:  $^1\text{H-NMR}$   $\delta$  5.67-5.58 (m, 1H), 4.83 (dd,  $J = 10.4$  and 7.3 Hz, 2H), 2.05-2.01 (m, 1H), 1.28-1.19 (m, 6H), 0.91 (d,  $J = 6.7$  Hz, 3H), 0.82 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C-NMR}$   $\delta$  144.9 (CH), 112.1 ( $\text{CH}_2$ ), 37.7 (CH), 36.3 ( $\text{CH}_2$ ), 29.4 ( $\text{CH}_2$ ), 22.8 ( $\text{CH}_2$ ), 20.1 ( $\text{CH}_3$ ), 14.0 ( $\text{CH}_3$ ). Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 55°C for 20 min, retention times (min): 5.4 (minor) and 5.5 (major).

**(R)-3-ethylhept-1-ene (4d)**:<sup>14</sup> Reaction carried out using 5.0 mol%  $\text{CuBr}\cdot\text{SMe}_2$  and 6.0 mol% **2**. Reaction time: 12 h. Purification by column chromatography (2 : 98  $\text{Et}_2\text{O}$ /pentane) afforded a 100 : 0 mixture of **4d** and **5d** as a colorless oil. [99% conversion,<sup>12</sup> 93% ee].<sup>15</sup> **4d**:  $^1\text{H-NMR}$   $\delta$  5.51-5.42 (m, 1H), 4.92-4.86 (m, 2H), 1.80-1.77 (m, 1H), 1.37-1.15 (m, 8H), 0.85-0.78 (m, 6H);  $^{13}\text{C-NMR}$   $\delta$  143.4 (CH), 113.9 ( $\text{CH}_2$ ), 45.8 (CH), 34.4 ( $\text{CH}_2$ ), 29.4 ( $\text{CH}_2$ ), 27.7 ( $\text{CH}_2$ ), 22.8 ( $\text{CH}_2$ ), 14.1 ( $\text{CH}_3$ ), 11.6 ( $\text{CH}_3$ ); LRMS (EI)  $m/z$  126 ( $\text{M}^+$ , 3), 97 (18), 84 (72), 69 (81), 55 (100). Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 55°C for 20 min, retention times (min): 9.8 (minor) and 9.9 (major).

**(-)-1-((S)-pent-1-en-3-yl)naphthalene (4e)**:<sup>10a,16</sup> Reaction time: 4h. Purification by column chromatography (2 : 98  $\text{Et}_2\text{O}$ /pentane) afforded a 87 : 13 mixture of **4e** and **5e** as a colorless oil. [86% yield, 90% ee,  $[\alpha]_D = -26$  ( $c$  1.0,  $\text{CHCl}_3$ )]. **4e**:  $^1\text{H-NMR}$   $\delta$  8.12 (d,  $J = 8.1$  Hz, 1H), 7.84 (d,  $J = 7.9$  Hz, 1H), 7.70 (d,  $J = 7.9$  Hz, 1H), 7.51-7.36 (m, 4H), 6.11-6.02 (m, 1H), 5.11-5.07 (m, 2H), 4.01 (q,  $J = 7.1$  Hz, 1H), 1.95-1.88 (m, 2H), 0.95 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C-NMR}$   $\delta$  142.8 (CH), 141.5 (C), 135.3 (C), 132.9 (C), 130.0 (CH), 127.7 (CH), 126.7 (CH), 126.6 (CH), 126.4 (CH), 125.0 (CH), 124.5 (CH), 115.7 ( $\text{CH}_2$ ), 47.1 (CH), 29.1 ( $\text{CH}_2$ ), 13.5 ( $\text{CH}_3$ ); LRMS (EI)  $m/z$  196 ( $\text{M}^+$ , 26),

<sup>11</sup> T. L. Underiner, S. D. Paisley, J. Schmitter, L. Lesheski, H. L. Goering, *J. Org. Chem.*, 1989, **54**, 2369.

<sup>12</sup> Conversion based on GC. The high volatility of the products **4c** and **4d** did not allow to completely remove the solvents after the chromatography, impeding the calculation of an accurate isolated yield.

<sup>13</sup> With 1.0 mol%  $\text{CuBr}\cdot\text{SMe}_2$  and 1.12 mol% **2** the product **4c** was obtained with 99% conversion, a regioselectivity of 100: 0, but a slightly lower enantioselectivity (84% vs. 92%ee).

<sup>14</sup> A. Pelter, K. Smith, S. Elgendy, M. Rowlands, *Tetrahedron Lett.*, 1989, **30**, 5647.

<sup>15</sup> With 1.0 % $\text{CuBr}\cdot\text{SMe}_2$  and 1.1 % **2**, **4d** was obtained with 99% conversion, 97 : 3 regioselectivity and 88% ee.

<sup>16</sup> A. O. Larsen, W. Leu, C. N. Oberhuber, J. E. Campbell, A. H. Hoveyda, *J. Am. Chem. Soc.*, 2004, **126**, 11130.

152 (42), 139 (11), 115 (14). Enantioselectivity determined by chiral HPLC analysis, Chiralcel OD-H (99.75% heptane/*i*PrOH), 40°C, retention times (min): 20.4 (major) and 23.2 (minor).

**1-Chloro-4-((*S*)-pent-1-en-3-yl)benzene (4f):**<sup>10a</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 82 : 18 mixture of **4f** and **5f** as a colorless oil. [80% yield, 96% ee] **4f**: <sup>1</sup>H-NMR δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 5.88 (m, 1H), 5.00 (m, 2H), 3.10 (dt, *J* = 7.7 and 7.3 Hz, 1H), 1.69 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 50°C, then 10°C/min to 120 °C (final temp) for 30 min, retention times (min): 19.7 (minor) and 20.1 (major).

**(+)-1-((*S*)-hept-1-en-3-yl)benzene (4g):**<sup>10a,17</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 87 : 13 mixture of **4g** and **5g** as a colorless oil. [92% yield, 94% ee, [α]<sub>D</sub> = +47 (*c* 0.5, CHCl<sub>3</sub>), lit.<sup>10a</sup> (88% ee) [α]<sub>D</sub> = + 44 (*c* 0.1, CHCl<sub>3</sub>)]. **4g**: <sup>1</sup>H-NMR δ 7.21 (m, 5H), 5.95 (m, 1H), 5.02 (m, 2H), 3.32 (q, *J* = 7.5 Hz, 1H), 1.70 (q, *J* = 7.4 Hz, 2H), 1.39-1.02 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C-NMR δ 144.7, 142.5, 128.4, 127.6, 126.0, 113.8, 49.9, 35.1, 29.7, 22.6, 14.0. Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 80 °C for 60 min, then 10 °C/min to 140 °C (final temp), retention times (min): 53.7 (minor) and 54.2 (major); retention time **5g**: 70.4 min.

**(+)-1-((*S*)-hepta-1,6-dien-3-yl)benzene (4h):**<sup>10b,c</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 91 : 9 mixture of **4h** and **5h** as a colorless oil. [93% yield, 95% ee, [α]<sub>D</sub> = +36 (*c* 1.5, CHCl<sub>3</sub>), lit.<sup>10b</sup> (92% ee) [α]<sub>D</sub> = + 33 (*c* 1.0, CHCl<sub>3</sub>)]. **4h**: <sup>1</sup>H-NMR δ 7.30-7.16 (m, 5H), 5.95 (m, 1H), 5.79 (m, 1H), 5.03-4.92 (m, 4H), 3.26 (q, *J* = 7.5 Hz, 1H), 2.10-1.94 (m, 2H), 1.81-1.75 (m, 2H); <sup>13</sup>C-NMR δ 144.1 (C), 142.1 (CH), 138.4 (CH), 128.4 (CH), 127.6 (CH), 126.1 (CH), 114.6 (CH<sub>2</sub>), 114.1 (CH<sub>2</sub>), 49.1 (CH), 34.4 (CH<sub>2</sub>), 31.5 (CH<sub>2</sub>); LRMS (EI) *m/z* 172 (M<sup>+</sup>, 13), 159 (6), 130 (33), 117 (100), 115 (41), 91 (48); HRMS Calcd. for C<sub>13</sub>H<sub>16</sub> 172.12520, found 172.12554. Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 90°C for 45 min, then 5 °C/min to 140 °C (final temp), retention times (min): 30.0 (minor) and 30.3 (major); retention time **5h**: 56.0 min.

**(-)-1-((*S*)-but-3-en-2-yl)naphthalene (4i):**<sup>9b,16,18</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 100 : 0 mixture of **4i** and **5i** as a colorless oil. [87% yield, 96% ee, [α]<sub>D</sub> = - 29.8 (*c* 1.1, CHCl<sub>3</sub>); lit.<sup>16</sup> [α]<sub>D</sub> = - 29 (*c* 1.0, CHCl<sub>3</sub>); lit.<sup>18a</sup> [α]<sub>D</sub> = - 37 (neat); lit.<sup>9b</sup> for (*R*)-**4i** (90% ee) +16.3 (*c* 0.4, CHCl<sub>3</sub>)]. **4i**: <sup>1</sup>H-NMR δ 8.15 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.54-7.41 (m, 4H), 6.23-6.15 (m, 1H), 5.17-5.13

<sup>17</sup> (a) A. Yanagisawa, N. Nomura, H. Yamamoto, *Tetrahedron* 1994, **50**, 6017. (b) J. J. Van Veldhuizen, J. E. Campbell, R. E. Giudici, A. H. Hoveyda, *J. Am. Chem. Soc.*, 2005, **127**, 6877.

<sup>18</sup> (a) R. Menicagli, O. Piccolo, L. Lardicci, M. L. Wis, *Tetrahedron*, 1979, **35**, 1301. (b) Y. Obora, Y. Tsuji, *J. Org. Chem.* 1995, **60**, 4647.

(m, 2H), 4.36-4.29 (m, 1H), 1.54 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$ -NMR  $\delta$  142.9 (CH), 141.4 (C), 134.0 (C), 131.4 (C), 128.9 (CH), 126.8 (CH), 125.7 (CH), 125.6 (CH), 125.3 (CH), 123.6 (CH), 123.5 (CH), 113.6 (CH<sub>2</sub>), 37.8 (CH), 20.2 (CH<sub>3</sub>); LRMS (EI)  $m/z$  182 ( $\text{M}^+$ , 50), 167 (100), 165 (31), 152 (24), 84 (27), 51 (11); HRMS Calcd. for  $\text{C}_{14}\text{H}_{14}$  182.10955, found 182.11070. Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 120°C for 60 min, retention times (min): 35.8 (minor) and 36.3 (major); retention time **5i**: 56.3 min.

**(+)-1-((S)-but-3-en-2-yl)-4-chlorobenzene (4j):**<sup>19</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 99 : 1 mixture of **4j** and **5j** as a colorless oil. [95% yield, 97% ee,  $[\alpha]_{\text{D}} = +12$  ( $c$  1.6, CHCl<sub>3</sub>)]. **4j**:  $^1\text{H}$ -NMR  $\delta$  7.29 (d,  $J = 8.5$  Hz, 2H), 7.07 (d,  $J = 8.5$  Hz, 2H), 6.00-5.90 (m, 1H), 5.06-4.97 (m, 2H), 3.44-3.36 (m, 1H), 1.32 (d,  $J = 7.0$  Hz, 3H); LRMS (EI)  $m/z$  166 ( $\text{M}^+$ , 47), 165 (9), 151 (46), 139 (10), 131 (68), 91 (100); HRMS Calcd. for  $\text{C}_{10}\text{H}_{11}\text{Cl}$  166.05492, found 166.05570. Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 95°C for 45 min, then 2°C/min to 140 °C (final temp), retention times (min): 25.8 (minor) and 26.1 (major); retention time **5j**: 40.8 min.

**(+)-Methyl 4-((S)-but-3-en-2-yl)benzoate (4k):**<sup>20</sup> Reaction time: 4h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 98 : 2 mixture of **4k** and **5k** as a colorless oil. [94% yield, 97% ee,  $[\alpha]_{\text{D}} = +12$  ( $c$  0.9, CHCl<sub>3</sub>)]. **4k**:  $^1\text{H}$ -NMR  $\delta$  7.91 (d,  $J = 8.30$  Hz, 2H), 7.22 (d,  $J = 8.30$  Hz, 2H), 5.97-5.90 (m, 1H), 5.03-4.98 (m, 2H), 3.84 (s, 3H), 3.49-3.44 (m, 1H), 1.32 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$ -NMR  $\delta$  167.0 (C), 150.9 (C), 142.2 (CH), 129.7 (CH), 128.0 (C), 127.2 (CH), 113.8 (CH<sub>2</sub>), 51.9 (CH<sub>3</sub>), 43.1 (CH), 20.5 (CH<sub>3</sub>); LRMS (EI)  $m/z$  190 ( $\text{M}^+$ , 44), 159 (33), 131 (100), 115 (25), 91 (22), 59 (8); HRMS Calcd. for  $\text{C}_{12}\text{H}_{14}\text{O}_2$  190.09937, found 190.09969. Enantioselectivity determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 105 °C for 70 min, then 1°C/min to 140 °C (final temp), retention times (min): 71.7 (minor) and 72.1 (major); retention time **5k**: 93.8 min.

**(-)-(((S)-2-methylbut-3-enyloxy)methyl)benzene (4l):**<sup>21</sup> Reaction time: 12 h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 100 : 0 mixture of **4l** and **5l** as a colorless oil. [93% yield, 92% ee,  $[\alpha]_{\text{D}} = -6$  ( $c$  1.1, CHCl<sub>3</sub>); lit.<sup>21a</sup>  $[\alpha]_{\text{D}} = -3$  ( $c$  1.0, CHCl<sub>3</sub>)]; **4l**:  $^1\text{H}$ -NMR  $\delta$  7.32 (d,  $J = 4.5$  Hz, 4H), 7.29-7.21 (m, 1H), 5.83-5.74 (m, 1H), 5.07-4.99 (m, 2H), 4.50 (s, 2H), 3.36 (dd,  $J = 9.1$  and 6.5 Hz, 1H), 3.28 (dd,  $J = 9.1$  and 6.8 Hz, 1H), 2.52-2.44 (m, 1H), 1.03 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$ -NMR  $\delta$  141.3 (CH), 138.6 (C), 128.3 (CH), 127.5 (CH), 127.4 (CH), 114.0 (CH<sub>2</sub>), 75.0 (CH<sub>2</sub>), 72.9 (CH<sub>2</sub>), 37.8 (CH), 16.6 (CH<sub>3</sub>); LRMS (EI)  $m/z$  176 ( $\text{M}^+$ , 12), 175 (5), 92 (11), 91 (100), 65 (7); HRMS Calcd. for  $\text{C}_{12}\text{H}_{16}\text{O}$  176.12011, found 176.12262. Enantioselectivity

<sup>19</sup> (a) G. Franciò, F. Faraone, W. Leitner, *J. Am. Chem. Soc.*, 2002, **124**, 736. (b) K. Tissot-Croset, A. Alexakis, *Tetrahedron Lett.*, 2004, **45**, 7375.

<sup>20</sup> P. Gomes, C. Gosmini, J. Périchon, *J. Org. Chem.*, 2003, **68**, 1142.

<sup>21</sup> (a) H. Lebel, V. Paquet *J. Am. Chem. Soc.*, 2004, **126**, 320. (b) J. C. Grandguillot, F. Pouessac, *Tetrahedron*, 1991, **47**, 5133.

determined by chiral HPLC analysis, Chiralcel OD-H (99.75% heptane/*i*PrOH), 40°C, retention times (min): 10.9 (minor) and 11.2 (major).

**(+)-1-(((*S*)-2-ethylbut-3-enyloxy)methyl)benzene (4m):** Reaction time: 12 h. Purification by column chromatography (2 : 98 Et<sub>2</sub>O/pentane) afforded a 98 : 2 mixture of **4m** and **5m** as a colorless oil. [97% yield, 94% ee, [α]<sub>D</sub> = + 19 (*c* 1.1, CHCl<sub>3</sub>)]. **4m**: <sup>1</sup>H-NMR δ 7.30-7.21 (m, 5H), 5.66-5.57 (m, 1H), 5.06-5.01 (m, 2H), 4.47 (s, 2H), 3.35 (d, *J* = 6.5 Hz, 2H), 2.22 (m, 1H), 1.56-1.47 (m, 1H), 1.27-1.20 (m, 1H), 0.83 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C-NMR δ 140.0 (CH), 138.6 (C), 128.3 (CH), 127.5 (CH), 127.4 (CH), 115.6 (CH<sub>2</sub>), 73.6 (CH<sub>2</sub>), 73.0 (CH<sub>2</sub>), 45.7 (CH), 24.0 (CH<sub>2</sub>), 11.4 (CH<sub>3</sub>); LRMS (EI) *m/z* 190 (M<sup>+</sup>, 11), 189 (11), 123 (21), 105 (100), 91 (79), 77 (30); HRMS Calcd. for C<sub>13</sub>H<sub>18</sub>O 190.13576, found 190.13505. Enantioselectivity determined by chiral HPLC analysis, Chiralcel OD-H (99.75% heptane/*i*PrOH), 40°C, retention times (min): 9.9 (minor) and 10.9 (major).

**(-)-(*S,E*)-methyl 4-phenylpent-2-enoate (6):**<sup>22</sup> Following the general procedure, in a Schlenk tube equipped with septum and stirring bar, CuBr SM<sub>2</sub> (15.0 μmol, 3.08 mg) and ligand **2** (18.0 μmol, 12.4 mg) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (3.0 mL) and stirred under argon at room temperature for 10 min. The mixture was cooled to – 75 °C and MeMgBr (3.0 M solution in Et<sub>2</sub>O, 1.73 mmol, 0.575 ml) was added dropwise. Cinnamyl bromide **3a** (296 mg, 1.50 mmol) was then added dropwise over 15 min *via* a syringe pump at that temperature. Once the addition was complete the resulting mixture was further stirred at – 75 °C for 4h. The reaction was quenched by addition of MeOH (0.5 mL) and the mixture was allowed to reach rt. Then, aqueous NH<sub>4</sub>Cl solution (1M, 2 mL) was added to the mixture. The organic phase was separated, and the resulting aqueous layer is extracted with Et<sub>2</sub>O (0.5 mL, 3x). The combined organic phases were dried and concentrated to a yellow oil which was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) in a dried Schlenk tube. Methyl acrylate (645 mg, 7.5 mmol) and Hoveyda-Grubbs 2<sup>nd</sup> generation catalyst (18 mg, 0.03 mmol) were sequentially added producing a light green solution which was stirred for 36 h at rt. The mixture was then concentrated *in vacuo* to a dark brown oil. Purification of this residue by silica gel chromatography (2 : 98 to 5/ 95 Et<sub>2</sub>O/pentane) affords **6** as a colorless oil [66% yield, [α]<sub>D</sub> = – 20 (*c* 0.3, CHCl<sub>3</sub>)]; <sup>1</sup>H-NMR δ 7.29-7.25 (m, 2H), 7.21-7.14 (m, 3H), 7.07 (dd, *J* = 15.7 and 6.7 Hz, 1H), 5.77 (dd, *J* = 15.7 and 1.5 Hz, 1H), 3.67 (s, 3H), 3.61-3.54 (m, 1H), 1.38 (d, *J* = 7.1 Hz, 3H); <sup>13</sup>C-NMR δ 167.1, 152.9, 143.2, 128.6, 127.3, 126.7, 119.6, 51.4, 42.0, 20.1; LRMS (EI) *m/z* 190 (M<sup>+</sup>, 40), 159 (18), 131 (100), 91 (22), 51 (13); HRMS Calcd. for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub> 190.09937, found 190.09953.

### Enantioselective Catalytic Conjugate Addition of EtMgBr to (*S*)-**6**.<sup>23</sup>

<sup>22</sup> (a) J. M. Concellón, E. Bardales, *Org. Lett.*, 2002, **4**, 189. (b) D. B. Barma, A. Kundu, A. Bandyopadhyay, A. Kundu, B. Sangras, A. Briot, C. Mioskowski, J. R. Falck, *Tetrahedron Lett.* 2004, **45**, 5917.

<sup>23</sup> F. López, S. R. Harutyunyan, A. Meetsma, A. J. Minnaard, B. L. Feringa, *Angew. Chem., Int. Ed.*, 2005, **44**, 2752.



**(+)-(3*S*,4*S*)-methyl 3-ethyl-4-phenylpentanoate (7):** In a Schlenk tube CuBr  $\text{SMe}_2$  (8.0  $\mu\text{mol}$ , 1.62 mg) and ligand (*R,S*)-**1b** (9.4  $\mu\text{mol}$ , 5.60 mg) were dissolved in  $\text{CH}_2\text{Cl}_2$  (1.5 mL) and stirred under argon at room temperature for 10 min. The mixture was cooled to  $-75^\circ\text{C}$  and EtMgBr (3.0 M in  $\text{Et}_2\text{O}$ , 0.78 mmol) was added dropwise. After stirring for 5 min at that temperature a solution of **6** (30 mg, 0.16 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.25 mL) was added dropwise over 10 min. After stirring at  $-75^\circ\text{C}$  for 22 h, MeOH (0.25 mL) and  $\text{NH}_4\text{Cl}$  (1M, 2 mL) were sequentially added, and the mixture was warmed to rt. After extraction with  $\text{Et}_2\text{O}$  (0.5 mL, 3x), the combined organic phases were dried and concentrated to a yellow oil which was flash chromatographed (2 : 99  $\text{Et}_2\text{O}$ /pentane) to yield **7** as a colourless oil [81% yield, 98% de,  $[\alpha]_{\text{D}} = +25$  (*c* 0.2,  $\text{CHCl}_3$ )];  $^1\text{H-NMR}$   $\delta$  7.26-7.12 (m, 5H), 3.57 (s, 3H), 2.82-2.73 (m, 1H), 2.30-2.15 (m, 2H), 2.08-1.97 (m, 1H), 1.38-1.27 (m, 1H), 1.17 (d,  $J = 7.1$  Hz, 3H), 1.14-1.06 (m, 1H), 0.81 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C-NMR}$   $\delta$  174.1 (C), 145.6 (C), 128.2 (CH), 127.7 (CH), 126.0 (CH), 51.4 ( $\text{CH}_3$ ), 42.8 (CH), 41.4 (CH), 35.3 ( $\text{CH}_2$ ), 24.4 ( $\text{CH}_2$ ), 17.1 ( $\text{CH}_3$ ), 11.1 ( $\text{CH}_3$ ); LRMS (EI)  $m/z$  220 ( $\text{M}^+$ , 20), 189 (11), 146 (43), 105 (100) 57 (21); HRMS Calcd. for  $\text{C}_{14}\text{H}_{20}\text{O}_2$  220.14632, found 220.14572. Diastereoselectivity determined by Chiraldex G-TA column (30 m x 0.25 mm),  $100^\circ\text{C}$ , retention times (min): 59.6 (minor: 3*R*,4*S* and 3*S*,4*R*) and 62.4 (major, 3*S*,4*S*). Alternatively, the diastereoselectivity could also be determined by  $^1\text{H-NMR}$ , by integration of the 3.5 ppm signals corresponding to the methyl ester group.

**(+)-(3*R*,4*S*)-methyl 3-ethyl-4-phenylpentanoate (8):** Same procedure as above but using (*S,R*)-**1b** instead of (*R,S*)-**1b**. [84% yield, 92% de,  $[\alpha]_{\text{D}} = +6$  (*c* 0.6,  $\text{CHCl}_3$ )];  $^1\text{H-NMR}$   $\delta$  7.24-7.20 (m, 2H), 7.14-7.11 (m, 3H), 3.53 (s, 3H), 2.71-2.67 (m, 1H), 2.16-2.01 (m, 3H), 1.44-1.29 (m, 2H), 1.19 (d,  $J = 7.2$  Hz, 3H), 0.83 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C-NMR}$   $\delta$  174.0 (C), 145.6 (C), 128.2 (CH), 127.8 (CH), 126.1 (CH), 51.3 ( $\text{CH}_3$ ), 42.5 (CH), 41.8 (CH), 36.3 ( $\text{CH}_2$ ), 23.1 ( $\text{CH}_2$ ), 18.2 ( $\text{CH}_3$ ), 10.4 ( $\text{CH}_3$ ); LRMS (EI)  $m/z$  220 ( $\text{M}^+$ , 18), 189 (12), 146 (58), 105 (100); HRMS Calcd. for  $\text{C}_{14}\text{H}_{20}\text{O}_2$  220.14632, found 220.14621. Diastereoselectivity determined by Chiraldex G-TA column (30 m x 0.25 mm),  $100^\circ\text{C}$ , retention times (min): 59.6 (major: 3*R*,4*S*), 62.4 (minor: 3*S*,4*S*) and 63.3 (minor: 3*R*, 4*R*). Alternatively, the de could also be determined by  $^1\text{H-NMR}$ , by integration of the 3.57 and 3.53 ppm signals corresponding to the methyl ester groups of **7** and **8**.

**Note:** The conjugate addition of EtMgBr to (*S*)-**6**, following the procedure described above, but using *racemic*-**1b** instead of (*R,S*)-**1b** led to a 84 : 16 mixture of **7** and **8**, as deduced by GC [Chiraldex G-TA column (30 m x 0.25 mm),  $100^\circ\text{C}$ , retention times (min): 59.6 (minor: 3*R*,4*S* and 3*S*,4*R*) and 62.4 (major, 3*S*,4*S*)] and  $^1\text{H-NMR}$  [by integration of the 3.57 and 3.53 ppm signals corresponding to the methyl ester groups of **7** and **8** respectively], indicating a strong preference for the formation of the 1,2-*anti* product **7**.

**Influence of the copper source and Grignard halide in the enantioselective allylic alkylation of cinnamyl halides catalyzed by Taniaphos 2.**

